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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/029,579	05/06/98	LANDEGREN U	1209-122P

002292 HM12/0504
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EXAMINER	
SHUMAN, J	
ART UNIT	**PAPER NUMBER**
1636	13

DATE MAILED: 05/04/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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Office Action Summary

Application No.	Applicant(s)
09/029,579	Landegren
Examiner	**Group Art Unit**
Jon Shuman	1636

☒ Responsive to communication(s) filed on *Feb 15, 2000*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-7* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-7* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

Claims 1-7 are pending in the application.

This action is responsive to the amendments of 15 February 2000.

A rejection of record not repeated in this office action has been withdrawn.

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The filing date for the application should be 6 May 1998. The Oath indicates 6 March, 1998. Appropriate correction is required, as the filing date is the date that all of the requirements of 35 U.S.C. 371 have been met, and not the actual date of submission.

Specification

2. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F..R 1.821 (a) (1) and (a) (2). However, this application fails to comply with the requirements of 37 C.F.R. 1.821 through 1.825 for the reason(s) set forth on the attached Notice to Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicants should carefully review the specification to identify and properly label each sequence that is referred to within the specification, including drawings. Sequences in drawings can be identified with a SEQ ID NO: in the Brief Description of the Drawings for the figure or be present in the figure itself. If one or more sequences are referred to in the specification that are not present in the Sequence Listing, then a new Sequence Listing, a new CRF diskette containing the Sequence Listing and a new statement that the two are the same and include no new matter must be submitted in order to fully comply with the Sequence Rules. Specifically, the 30mer oligonucleotide presented at page 7 exceeds 10 nucleotides, and therefore must be presented in a sequence listing accompanied by a diskette containing the same.

Applicants are required to comply with all of the requirements of 37 C.F.R. 1.821 through 1.825. Any response to this Office Action which fails to meet all of these requirements will be considered non-responsive. The nature of the noncompliance with the requirements with 37 C.F.R. 1.821 through 1.825 did not preclude the continued examination of the application on the merits, the results of which are communicated below.

Response to Amendment

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

5. Applicant's arguments filed 15 February 2000 have been fully considered but they are not persuasive. Applicants claim a pharmaceutical composition for targeting a double stranded nucleic acid comprising a padlock probe oligonucleotide which catenates a target sequence and inhibits transcription. The term pharmaceutical is interpreted to encompass a treatment effect for the instant compositions. For full details of the rejection, please refer to the previous office action. To summarize, the art of using oligonucleotides to inhibit gene expression or replication is unpredictable with regards to targeting of differing sequences, with regards to reproducibility of results, with regards to specificity of the targeting, and with regards to toxicity of certain formulations. Whether the oligonucleotides function as antisense molecules, antigene molecules, triplex forming molecules, or clamps, they are oligonucleotide formulations intended for pharmaceutical applications and thus are analogous art. Applicants present examples of the use of the claimed compositions *in vitro*. In the first example, double stranded nucleic acid is the target.

In the second example, single stranded nucleic acid is the target. Given the state of the art for pharmaceutical oligonucleotide formulations, applicants must give sufficient guidance to instruct one of ordinary skill in the art in the making and use of the claimed compositions, commensurate with the full scope of the claims. Applicants present no evidence that the instant formulations are stable in vivo (not degraded), that they function equivalently in targeting specificity, or that they function by inhibition of gene expression or replication *in vivo*. Applicants assert (p 7) that the circularized oligonucleotides are nuclease resistant, but that "excess of padlock probes is rapidly degraded by exonucleases". Applicants do not teach the use of the compositions in order to avoid the nuclease activity, nor provide prophetic or exemplary teachings demonstrating efficacy of the compositions as pharmaceuticals. Applicants must teach one of ordinary skill in the art how to make and use an invention, commensurate with the full scope of the claims, without requiring undue and burdensome experimentation. The rejection is maintained.

Claim Rejections - 35 USC § 102

Claim 7 stand rejected as anticipated by the Nilsson reference.

In response to applicant's argument that Nilsson describes"several complexes between an oligonucleotide and certain nucleic acid molecules", a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process

of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Applicants assert that the padlock probes function by base pairing, bringing the ligatable ends into apposition for ligation. This is the same mechanism as disclosed in the Nilsson reference. The rejection is maintained.

Allowable Subject Matter

No claims are allowed.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Shuman whose telephone number is (703) 306-5819. The examiner can normally be reached on Monday to Friday from 8:00 AM to 4:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than 24 hours after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott, can be reached on (703) 308-4003. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Jon Shuman

1 May 2000

DAVID GUZO
PRIMARY EXAMINER